

REMARKS

Claims 1, 13, 22, 31, 34, 35, and 38 have been amended herein. Claims 11, 12, 20, 21, 29, 30, 33, and 37 have been canceled herein. Such cancellation is without prejudice to further prosecution of these claims on one or more continuing applications. Claims 1-10, 13-19, 22-28, 31-32, 34-37, and 38 remain in the application. Favorable reconsideration is respectfully requested.

Claims 1, 13, 22, 31, 34, 35, and 38 have been amended to recite that the isolated nucleic acid target defines a known or putative binding site for a “sequence-specific” regulatory factor. Verbatim support is provided in the specification at page 5, last paragraph; page 20, first paragraph; page 24, last paragraph; and in Example 7, beginning at the top of page 37.

Claims 1, 13, 22, 31, 34, and 35 have been amended to recite that the linker is “at least 30 Å long.” Verbatim support can be found in Claims 11, 20, 29, 33, and 37 as originally filed.

Claims 1, 13, 22, 31, and 38 have been amended to recite that the entropy of the linker is sufficiently large to confer “temperature-sensitive” conditional behavior to the linker. Verbatim support is provided at page 25, third full paragraph, and in Claims 12, 21, 30, 34, and 38 as originally filed.

No new matter added.

Regarding Claim 36, Applicant notes that this claim was not subject to any rejections in the first Office Action dated September 20, 2006, nor in the present Final Office Action. Claim 36 was earlier re-written as an independent claim. Applicant therefore submits that Claim 36 is now in condition for allowance. Notification of the status of Claim 36 is earnestly solicited.

Rejection of Claims 12, 21, 30, 34, and 38 Under §112, Second Paragraph:

As applied to Claims 12, 21, and 30, this rejection has been rendered moot by cancellation of the claims. Such cancellation is without prejudice on the merits.

As applied to Claims 34 and 38, this rejection is believed to have been overcome, in part, by appropriate amendment to the claims, and is, in part, respectfully traversed.

With respect to the phrase “conditional behavior,” this rejection is believed to have been overcome, in part, by noting that the conditional behavior is “temperature sensitive.” See page 25, lines 24-28:

Temperature sensitivity thus permits rapid spatio-temporal control of the activity of the test compound bonded to the linker. The utility of this approach is that the flexible linker will behave differently at different temperatures, due to the increased entropy inherent in a longer linker. This characteristic of entropically destabilized linkers is designated herein as “conditional behavior.”

Applicant further notes that the linker as recited in Claim 34 is positively recited as being at least 30 Å long. Applicant submits that these additional clarifications overcome, at least in part, the rejection made under §112, second paragraph.

With respect to the metes and bounds of the phrase “entropically destabilized” as used in the, Applicant respectfully submits that the term is clearly and explicitly defined at page 25 of the application as filed and easily understood by one of ordinary skill in the art. The linker is sufficiently long to act as a temperature-dependant “switch.” Again, see page 25 of the application as filed. As noted by the Office, an entropically destabilized linker falling within the scope of the claims is “temperature-sensitive.” Thus, as noted at the top of page 4 of the Office Action, a 1°C change in temperature may very well result in the conditional behavior required by the claims. But the Office has failed to articulate how that outcome is in any way ambiguous or unclear. It is well within ambit of an ordinarily skilled biochemist to conduct delicate experiments where the temperature is controlled with within fractions of a degree. There is nothing ambiguous or even difficult about running the same method falling within the scope of the claims in triplicate: once at a first temperature of, say, 35°C, again at a second temperature of 36°C, and again at a third temperature of 37°C. The results would then be compared to see if the linker behaved differently at 36°C or 37°C, as compared to 35°C.

Applicant explicitly intends this to be the case. As positively recited in the claims, the linker confers “temperature-sensitive, conditional behavior” on the isolated nucleic acid target.

Applicants thus submit that this rejection is now untenable. Withdrawal of the rejection is respectfully requested.

**Rejection of Claims 1-10, 13-19, and 31-32 Under §102(b) in View of Ansari et al. (2001)
Chem. Biol., 8:583-592, Published Online on May 8, 2001:**

This rejection is believed to have been overcome by amendment to the claims. Specifically, the subject matter of Claims 11 and 12 has been inserted into Claim 1. Because

Claims 11 and 12 were not subject to this rejection, the rejection as applied to Claim 1 and the claims dependent on Claim 1 has been overcome.

Likewise, the subject matter of Claims 20 and 21 has been inserted into independent Claim 13. Because Claims 20 and 21 were not subject to this rejection, the rejection as applied to Claim 13 and the claims dependent on Claim 13 has been overcome.

Lastly, the subject matter of Claim 33 has been inserted into independent Claim 31. Because Claim 33 was not subject to this rejection, the rejection as applied to Claims 31 and 32 has been overcome.

Applicants also note that the claims as amended do not extend to transcriptional machinery. Claim 1, for example, has been amended to require an isolated nucleic acid target that defines at least one known or putative binding site for a “sequence specific” regulatory factor. Insofar as the transcriptional machinery is not sequence-specific, the claims as amended are clearly distinct from the artificial transcription activator described in the Ansari et al. paper.

For these reasons, Applicant submits that the rejection of Claims 1-10, 13-19, and 31-32 under §102(b) in view of Ansari et al. has been overcome. Withdrawal of the rejection is respectfully requested.

Rejection of Claims 22-28 Under §102(b) in View of Ansari et al. (2001), with Additional Evidence Provided by Sadowski et al. (1998) *Nature*, 335:563-564:

This rejection has been overcome by amendment to the claims. Specifically, the subject matter of claims 29 and 30 has been incorporated into independent Claim 22. Neither of Claims 29 nor 30 were made subject to this rejection. Thus, by incorporating this subject matter into Claim 22, the rejection of independent Claim 22 and dependent Claims 23-28 has been overcome.

Applicant thus submits that the rejection of Claims 22-28 under §102(b) in view of Ansari et al., with additional evidence provided by Sadowski et al. has been overcome. Withdrawal of the rejection is respectfully requested.

Rejection of Claims 1-4, 8-9, 11, 13, 17-18, 20, 31, 33, 35, and 37 Under §102(e) in View of Stanojevic, U.S. Patent Application Pub. No. 2003/105,045:

As applied to Claims 11, 20, 33, and 37, this rejection has been rendered moot by cancellation of the claims.

As applied to the remaining claims, this rejection has been overcome by amendment to the claims.

Specifically, the subject matter of Claim 12 has been inserted into Claim 1. Claim 12 was not made subject to this rejection. Thus, by amending Claim 1 to include the subject matter of Claim 12, the rejection of Claims 1-4, 8, and 9 has been overcome.

The subject matter of Claim 21 has been inserted into Claim 13. Claim 21 was not made subject to this rejection. Thus, by amending Claim 13 to include the subject matter of Claim 21, the rejection of Claims 13, 17, and 18 has been overcome.

Claim 31 has been amended to include the subject matter of Claim 33, as well as the temperature-sensitive, conditional behavior of the linker as recited in Claim 21 as originally filed. As noted in the immediately preceding paragraph, Claim 21 was not made subject to this rejection. Therefore, by amending Claim 31 to include the subject matter of Claim 21, the rejection of Claims 31 has been overcome.

Claim 35 has been amended to include the subject matter of Claim 37. Claim 37 has also been amended to recite that the isolated nucleic acid target defines a “sequence-specific” regulatory factor binding site. Insofar as Stanojevic does not describe a kit having such a nucleic acid target, Applicants submits that this rejection has been overcome.

In light of the amendments to the claims, Applicant submits that the rejection of Claims 1-4, 8-9, 11, 13, 17-18, 20, 31, 33, 35, and 37 under §102(e) in view of Stanojevic is has been overcome. Withdrawal of the rejection is respectfully requested.

Rejection of Claims 1, 3-4, 8-10, 13, 15, 17-19, 22, 26-28, and 31-32 Under §102(a) in View of Stanojevic & Young (2002) *Biochem.*, 41:7209-7216:

This rejection has been overcome by amendment to the claims.

The subject matter of Claims 11 and 12 has been inserted into Claim 1. Because Claims 11 and 12 were not subject to this rejection, the rejection as applied to Claims 1, 3-4, and 8-10 has been overcome.

The subject matter of Claims 20 and 21 has been inserted into independent Claim 13.

Because Claims 20 and 21 were not subject to this rejection, the rejection as applied to Claims 13, 15, and 17-19 has been overcome.

The subject matter of Claims 29 and 30 has been incorporated into Claim 22. Claims 29 and 30 were not made subject to this rejection. Thus, this amendment overcomes this rejection as it has been applied to Claims 22 and 26-28.

The subject matter of Claim 33 has been inserted into independent Claim 31. Because Claim 33 was not subject to this rejection, the rejection as applied to Claims 31 and 32 has been overcome.

In light of the amendment to the claims, Applicant submits that the rejection of Claims 1, 3-4, 8-10, 13, 15, 17-19, 22, 26-28, and 31-32 under §102(a) in view of Stanojevic & Young has been overcome. Withdrawal of the rejection is respectfully requested.

Rejection of Claims 1, 11, 13, 20, 31, and 33 Under §103(a) over Ansari et al. (2001) in View of Arora et al. (2002) *J. Am. Chem. Soc.*, 124:13067-13071:

As applied to Claims 11, 20 and 33, this rejection has been rendered moot by cancellation of the claims.

As applied to Claim 1, this rejection has been overcome by inserting the subject matter of Claim 12 into Claim 1. Because Claim 12 was not subject to this rejection, the rejection as applied to Claim 1 has been overcome.

The subject matter of Claim 21 has been inserted into independent Claim 13. Because Claim 21 was not subject to this rejection, the rejection as applied to Claim 13 has been overcome.

Likewise, Claim 31 has been amended to include the temperature-sensitive conditional behavior recited in Claim 21. Thus the rejection as applied to Claim 31 has also been overcome.

Withdrawal of the rejection is respectfully requested.

Rejection of Claims 1, 3, 6-9, 13, and 15-18 Under §103(a) over Ansari et al. (2001) in View of Ansari et al. (2002) *Curr. Opin. Chem. Biol.*, 6:765-772:

This rejection has been overcome by amendment to the claims.

The subject matter of Claims 11 and 12 has been inserted into Claim 1. Because Claims

11 and 12 were not subject to this rejection, the rejection as applied to Claims 1, 3, and 6-9 has been overcome.

The subject matter of Claims 20 and 21 has been inserted into independent Claim 13. Because Claims 20 and 21 were not subject to this rejection, the rejection as applied to Claims 13 and 15-18 has been overcome.

In light of the amendment to the claims, Applicant submits that the rejection of Claims 1, 3, 6-9, 13, and 15-18 under §103(a) over Ansari et al. (2001) in view of Ansari et al. (2002) has been overcome. Withdrawal of the rejection is respectfully requested.

Rejection of Claims 22 and 29 Under §103(a) over Ansari et al. (2001), in View of Sadowski et al. and Arora et al.:

As applied to Claim 29, this rejection has been rendered moot by cancellation of the claims.

As applied to Claim 22, this rejection has been overcome by inserting the subject matter of Claim 30 into Claim 22. Claim 30 was not made subject to this rejection. Thus, the amendment to Claim 22 to include the subject matter of Claim 30 overcomes this rejection.

Applicant therefore submits that the rejection of Claim 22 under §103(a) over Ansari et al. (2001), in view of Sadowski et al. and Arora et al. has been overcome. Withdrawal of the rejection is respectfully requested.

Rejection of Claims 22 and 24-27 Under §103(a) over Ansari et al. (2001) in View of Sadowski et al. and Ansari et al. (2002):

The subject matter of Claims 29 and 30 has been incorporated into Claim 22. Claims 29 and 30 were not made subject to this rejection. Thus, this amendment overcomes this rejection as it has been applied to Claims 22 and 24-27.

Applicant therefore submits that the rejection of Claims 22 and 24-27 under §103(a) over Ansari et al. (2001) in view of Sadowski et al. and Ansari et al. (2002) has been overcome. Withdrawal of the rejection is respectfully requested.

Rejection of Claims 1, 3, 8-9, 11, 13, 17-18, 20, 31, and 33 Under §103(a) over Felgner et al. (U.S. Patent No. 6,165,720) in view of Arora et al.:

As applied to claims 11, 20, and 33, this rejection has been rendered moot by cancellation of the claims.

This rejection as applied to the remaining claims has been overcome by appropriate amendment.

The subject matter of Claim 12 has been inserted into Claim 1. Because Claim 12 was not subject to this rejection, the rejection as applied to Claims 1, 3-4, and 8-10 has been overcome.

The subject matter of Claim 21 has been inserted into independent Claim 13. Because Claim 21 was not subject to this rejection, the rejection as applied to Claims 13, 17, and 18 has been overcome.

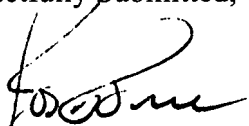
Likewise, Claim 31 has been amended to include the temperature-sensitive conditional behavior recited in Claim 21. Thus the rejection as applied to Claim 31 has also been overcome.

Applicant therefore submits that the rejection of Claims 1, 3, 8-9, 11, 13, 17-18, 20, 31, and 33 under §103(a) over Felgner et al. in view of Arora et al. has been overcome. Withdrawal of the rejection is respectfully requested.

CONCLUSION

In light of the above amendment and accompanying remarks, Applicant submits that the application is now in condition for allowance. Early notification of such action is earnestly solicited. If any questions arise, please contact the undersigned attorney. Telephone calls related to this application are welcomed and encouraged. The Commissioner is authorized to charge any fees or credit any overpayments relating to this application to deposit account number 18-2055.

Respectfully Submitted,



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